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L1 STRUCTURE UPLOADED

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L3 28 SEA SSS FUL L1

=> file ca

=> s 13

L4 3 L3

=> d ibib abs hitstr 1-3

L4 ANSWER 1 OF 3 CA
CCESSION NUMBER:
10016568 CA 140:16568 CA 140:1656

DOCUMENT TYPE: Patent English 3

LANGUAGE: FAMILY ACC. NUM. COUNT: FATENT INFORMATION:

PATENT NO.	KIND	DATE		APPLICATION NO	٠.	DATE
US 2003229058	A1	20031211		US 2003-43176	2	20030508
US 6670376	В1	20031230		US 2002-29283	5	20021112
US 2004059116	A1	20040325		US 2003-64292	5	20030818
US 2004063755	A1	20040401		US 2003-64319	6	20030818
PRIORITY APPLN. INFO.			US	2001-338194P	P	20011113
			US	2001-343771P	P	20011228
			US	2002-292835	A2	20021112
			US	2002-292211	A1	20021112
OTHER SOURCE(S):	MA	RPAT 140:165	68			

ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)
(prepn. of aryl aniline .beta.-2 adrenergic receptor agonists for
treatment of pulmonary disorders)
53064-66-3 CA
2(1H)-Quinolinone, 5-f(1R)-2-f(2-f4-f(6-ethoxy[1,1'-biphenyl]-3yl)amino]phenyl]ethyl]amino]-1-hydroxyethyl)-8-hydroxy- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

530084-87-8 CA 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

530117-33-0 CA 2(1H)-Quinolinone, 8-hydroxy-5-[1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

Title compds. I [R1-5 = H, alk(en/yn)yl, cycloalkyl, heterocyclyl, etc.; R6 = H, alkyl, alkoxy; R7 = H, alkyl; R8 = H, alkyl; R9 = alk(en/yn)yl, (heterolaryl, etc.; R10 = H, alkyl; R1-13 = H, (cyclo)alkyl, alkenyl, alkenyl, etc.; ps = 0-4] are prepd. For instance, the di-Me ketal of 4-hydroxy-3-hydroxymethyl-.alpha.-bromocactophenone (prepn. given) is reacted with 4-bromophenethylamine (CHZC12, ELSN) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NaBH4). The resulting protected amino alc. is then coupled with N-(4-heptyl-6-methyl-2-pyrimidinyl)sulfanllamide (PhMe, dppf, Pd2dba3, 80.degree., 5 h) and then deprotected with NGAC (80.degree., 5 h) to give II. All of the compds. tested demonstrated greater binding at the a.2

a.2 adrenergic receptor than at the .beta.1 adrenergic receptor, i.e., Ki(.beta.1) > Ki(.beta.2); many with a selectivity greater than 20. I

useful for the treatment of pulmonary diseases.
530084-66-39 530084-67-89 530117-33-0F
530117-43-29 530118-10-69 530118-11-79
530118-12-98 530118-13-99 530118-17-39
530118-12-95 530118-22-99
530118-24-29 530118-22-39 61318-18-319
631915-04-39 631915-05-49 631915-06-59
631915-07-96 631915-06-79 631915-09-89
631915-10-19
FUL PRC (Pharmacological activity): SPN (Synthete IT

SINE-10-17
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

PAGE 2-A

530117-43-2 CA 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-biphenyl]-3-y1)amino]phenyl]ethyl]amino]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued

●x HCl

RN 530118-10-6 CA
CN [1,1'-Biphenyl]-3-carbonitrile,
5'-[[4-[2-[(2R)-2-(1,2-dihydro-8-hydroxy2-oxo-5-quinolinyl)-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy(901) (CA YNDEX NAME)

Absolute stereochemistry.

RN 530118-11-7 CA
CN [1,1'-Biphenyl]-3-carbonitrile,
5'-[4-[2-[(2R)-2-(1,2-dihydro-8-hydroxy2-oxo-5-quinolinyl]-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy-,
trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued

RN 530118-13-9 CA
CN 2(1H)-Quinolinone, 5-[(1R)-2-[(2-[4-[(4'-(aminomethyl)-6-methoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy-, trifluoroacetate (sait) (9CI) (CA INDEX NAME)

CM 1

CRN 530118-12-8 CMF C33 H34 N4 O4

Absolute stereochemistry.

CM 2

CRN 76-05-1 CMF C2 H F3 O2 L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued) CRN 530118-10-6 CMF C33 H30 N4 O4

Absolute stereochemistry.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

F-C-C02H

RN 530118-12-8 CA
CN 2(1H)-Quinolinone, 5-{(1R)-2-[(2-{4-[[4'-(aminomethyl)-6-methoxy[1,1'-biphenyl]-3-yl]amino]phenyl)ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

RN 530118-17-3 CA
CN [1,1'-Biphenyl]-4-carboxaldehyde, 5'-[[4-[2-[[(2R)-2-(1,2-dihydro-8-hydroxy-2-oxo-5-quinolinyl]-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 530118-16-2 CMF C33 H31 N3 O5

Absolute stereochemistry.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

F−С− со<sub>2</sub>н

RN 530118-19-5 CA
CN 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[[6-methoxy-4'(methylsulfonyl)[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]ethyl]-,
trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 530118-18-4

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN CMF C33 H33 N3 O6 S (Continued)

Absolute stereochemistry.

F-C-CO2H

530118-20-8 CA 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[(4'-hydroxy-6-methoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.

RN 530118-25-3 CA
CN 2(1H)-Quinolinone,
5-[(1R)-2-[(2-[4-{(3'-chloro-6-methoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy-, trifluoroacetate
(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 530118-24-2 CMF C32 H30 C1 N3 O4

Absolute stereochemistry.

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

530118-21-9 CA 2[IR]-Quinolinone, 8-hydroxy-5-[[IR]-1-hydroxy-2-[[2-[4-[(4'-hydroxy-6-methoxy[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]ethyl]-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 530118-20-8 CMF C32 H31 N3 O5

Absolute stereochemistry.

CM

CRN 76-05-1 CMF C2 H F3 O2

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

CM 2

CRN 76-05-1 CMF C2 H F3 O2

N 631914-89-1 CA N 2[1H]-Quinolinone, -hydroxy-5-[(1R]-1-hydroxy-2-[[2-[4-[[6-methoxy-4'-(4-morpholiny]methyl][1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]ethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

RN 631915-04-3 CA
CN [1,1'-Biphenyl]-3-carboxamide,
5'-[4-[2-[((ZR)-2-(1,2-dihydro-8-hydroxy-2oxo-5-quinolinyl]-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 631915-05-4 CA
CN 2(1H)-Quinolinone, 5-[(1R)-2-[[2-[4-[[3'-{aminomethyl})-6-methoxy[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

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RN 631915-07-6 CA
CN 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[(2-[4-[[6-methoxy-3'[[[phenylmethyl]amino]methyl][1,1'-biphenyl]-3yl]amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

RN 631915-08-7 CA
CN 2(1H)-Quinolinone, 5-[(1R)-2-[[2-[4-[[3'-[(dimethylamino)methyl]-6-methoxy[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

•x HCl

RN 631915-06-5 CA
CN 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[[6-methoxy-3'[[1-methylethyl]amino]methyl][1,1'-biphenyl]-3yl]amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

14 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

=:0

RN 631915-09-8 CA

2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[[6-methoxy-3'-([(3-pyridinylmethyl)amino]methyl][1,1'-biphenyl]-3yl]amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

PAGE 2-A

631915-10-1 CA 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[[6-methoxy-3'-[[[4-methoxyphenyl]methyl]amino]methyl][1,1'-biphenyl]-3- yl]amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 3 CA
CCESSION NUMBER:
138:401502 CA
Freparation of aryl aniline .beta.-2 adrenergic
receptor agonists
INVENTOR(S):
Moran, Edmund J.; Jacobsen, John R.; Leadbetter,
Michael R.; Nodwell, Matthew B.; Trapp, Sean G.;
Aggen, James: Church, Timothy J.
PATENT ASSIGNEE(S):
SOURCE:
CODEN: PIXXD2
DOCUMENT TYPE:
LANGUAGE:
PAMILY ACC. NUM. COUNT:
3

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2003042164 A1 20030522 WO 2002-US36237 20021112

W: AE, AG, AL, AM, AT, AU, AZ, BB, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, II, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LK, LS, LT, LU, LV, MA, MD, MG, MG, MK, MN, MN, MX, MZ, NO, NZ, OM, FK, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, TT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, CQ, GW, ML, MR, NE, SN, TD, TS

US 2004059116 A1 20040325 US 2001-338194P P 20011128 

OTHER SOURCE(S):

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

PAGE 2-A

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

Title compds. I [R1-5 = H, alk(en/yn)yl, cycloalkyl, heterocyclyl, etc.; R6 = H, alkyl, alkoxy; R7 = H, alkyl; R8 = H, alkyl; R9 = alk(en/yn)yl, (heterolaryl, etc.; R10 = H, alkyl; R1-13 = H, (cyclo)alkyl, alkenyl, alkynyl, (heterolaryl, etc.; p = 0-4) are prepd. For instance, the di-Me ketal of 4-hydroxy-3-hydroxymethyl-alpha.-bromoacetophenone (prepn. given) is reacted with 4-bromophenethylamine (CHZC12, EL3N) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NABH4). The resulting protected amino alc. is then coupled with N-(4-heptyl-6-methyl-2-pyrimdinyl)sulfarilamide (PhMe, dppf, PdZdba3, 80.degree., 5 h) and then deprotected with HOAC (80.degree., 5 h) to give II. All of the compds. tested demonstrated greater binding at the acceptance of the compds.

adrenergic receptor than at the .beta.l adrenergic receptor, i.e., Ki(.beta.l) > Ki(.beta.2); many with a selectivity greater than 20. I

useful for the treatment of pulmonary diseases.
330084-85-3F 530084-97-9F 530117-13-0P
330127-43-2P 530118-11-19P 530118-11-7P
530118-12-9F 530118-13-9F 530118-17-3F
530118-12-9F 530118-22-3P
RL: PRC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BROL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aryl aniline .beta.-2 adrenergic receptor agonists for treatment of pulmonary disorders)
530084-66-3 CA
2(IH)-Quinolinone, 5-[(IR)-2-[[2-[4-[(6-ethoxy[1,1'-biphenyl]-3-yl)amino])-hydroxyethyl]-8-hydroxy- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN Absolute stereochemistry. (Continued)

Absolute stereochemistry.

530117-33-0 CA 2(1H)-Quinolinone, 8-hydroxy-5-[1-hydroxy-2-[(2-[4-[(6-methoxy{1,1'-biphenyl]-3-y1) amino]phenyl]ethyl]amino]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

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> > PAGE 2-A

PAGE 1-A

530117-43-2 CA 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-bipheny1]-3-y1)amino]pheny1]ethyl]amino]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

●x HCl

Absolute stereochemistry.

RN 530118-10-6 CA CN [1,1'-Biphenyl]-3-carbonitrile, 5'-[4-[2-[1(2R)-2-(1,2-dihydro-8-hydroxy-2-oxo-5-quinolinyl]-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy-(9CI) (CA INDEX NAME)

RN 530118-11-7 CA
CN [1,1'-Biphenyl]-3-carbonitrile,
5'-[[4-[2-[((2R)-2-(1,2-dihydro-8-hydroxy2-oxo-5-quinolinyl]-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy-,
trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CRN 530118-10-6 CMF C33 H30 N4 O4

Absolute stereochemistry.

Page 7

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN

CM 2

530118-12-8 CA 2(1H)-Quinolinone, 5-[(1R)-2-[[2-[4-[[4'-(aminomethyl)-6-methoxy[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI)(CA INDEX NAME)

Absolute stereochemistry.

530118-13-9 CA 2(1H)-Quinolinone, 5-[(1R)-2-[[2-[4-[[4\*-(aminomethyl)-6-methoxy[1,1\*-

ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued) biphenyl]-3-yl]amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CRN 530118-12-8 CMF C33 H34 N4 O4

Absolute stereochemistry.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

CO2H

530118-17-3 CA
[1,1'-Biphenyl]-4-carboxaldehyde, 5'-[[4-[2-[[(2R)-2-[1,2-dihydro-8-hydroxy-2-oxo-5-quinolinyl)-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CRN 530118-16-2 CMF C33 H31 N3 O5

Absolute stereochemistry.

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

CM 2

CRN 76-05-1 CMF C2 H F3 O2

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530118-20-8 CA 2(1H)-Quinolinne, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[(4'-hydroxy-6-methoxy[1,1'-biphenyl]-3-y1)amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Page 8

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN

CM 2

CRN 76-05-1 CMF C2 H F3 O2

530118-19-5 CA 2(1H)-Quinclinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[(2-[4-[(6-methoxy-4'-(methylsulfonyl)[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]ethyl]-, trifluoroscetate (salt) (9CI) (CA INDEX NAME)

CRN 530118-18-4 CMF C33 H33 N3 O6 S

Absolute stereochemistry.

ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued) 530118-21-9 CA 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[(4'-hydroxy-6-methoxy[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]ethyl]-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 530118-20-8 CMF C32 H31 N3 O5

Absolute stereochemistry.

2

со2н

RN 530118-24-2 CA
CN 2{1H}-Quinolinone,
5-[(1R)-2-[(2-[4-[3'-chloro-6-methoxy[1,1'-biphenyl]-3y1)amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

RN 530118-25-3 CA
CN 2(1H)-Quinolinone,
5[(1R)-2-[12-[4-[3'-chloro-6-methoxy[1,1'-biphenyl]-3y1)aminolphenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy-, trifluoroacetate
(salt) (9C1) (CA INDEX NAME)

CRN 530118-24-2 CMF C32 H30 C1 N3 O4

Absolute stereochemistry.

2

ACCESSION NUMBER:

TITLE:

ANSWER 3 OF 3 CA
SSSION NUMBER:
LE: 138:401501 CA
Preparation of aryl aniline .beta.-2 adrenergic receptor agonists
MOTAN, Edition of aryl aniline .beta.-2 adrenergic receptor agonists
MOTAN, Edmund J.; Jacobsen, John R.; Aggen, James
INT ASSIGNEE(S): Heravance, Inc., USA
PCT Int. Appl., 75 pp.
CODEN: PIXXD2
MENT TYPE: CODEN: PIXXD2
MINGE: Heravance, Inc., USA
PCT Int. Appl., 75 pp.
Edmin Type: Fixed Fixe INVENTOR (S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE:

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

OTHER SOURCE(S):

ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN

Title compds. I [R1 = methoxy, ethoxy; R2 = H, Ph or R1 = H and R2 = phenyl; R3 = CHZOH, NHCHO; R4 = H or R3-4 = taken together are NHC(O|CH=CH] are prepd. For instance, the di-Me ketal of 4-hydroxy-3-hydroxymethyl-.alpha.-bromoacetophenone (prepn. given) is reacted with 4-bromophenethylamine (CHZC12, EtN) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NaBH4). The resulting protected amino alc. is then coupled with 4-methoxy-3-phenylamiline (PhMe, dppf, PdZdba3, NaOBu-t, 80. degree., S h) and then deprotected with HOAC (80. degree., S h) to give II. All of the compds. tested demonstrated greater binding at the .beta.2 adrenergic receptor, i.e., Ki(.beta.1); many with a selectivity greater than 20. I are useful for the treatment of pulmonary diseases.

530084-34-5F 530084-35-6F 530084-43-6F
530084-39-8F 530084-65-F 530084-87-8F
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
[prepn. of aryl aniline .beta-2 adrenergic recentor againsts for

(Uses)

(prepn. of aryl aniline .beta,-2 adrenergic receptor agonists for treatment of pulmonary disorders)

530084-34-5 CA

2(1K)-Quinolinone, 8-hydroxy-5-[1-hydroxy-2-[(2-[4-[(6-methoxy[1,1'-biphenyl]-3-y1)amino]phenyl]ethyl]amino]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

PAGE 2-A

530084-35-6 CA 2[IR]-Quinolinone, 8-hydroxy-5-[[IR]-1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-biphenyl]-3-y1)amino}phenyl]ethyl]amino]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN

PAGE 2-A

530084-53-8 CA Z(1H)-Quinclinone, 5-[2-[{2-[4-[{6-ethoxy[1,1'-biphenyl]-3-y|})amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI) (CA INDEX NAME)

PAGE 1-A

L4 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

530084-43-6 CA 2(1H)-Quinolinone, 8-hydroxy-5-(1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-bipheny1]-3-y1)amino]pheny1]ethyl]amino]ethyl]- (9C1) (CA INDEX NAME)

PAGE 1-A

L4 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

530084-66-3 CA 2(1H)-Quinolinone, 5-{(1R)-2-[(2-[4-[(6-ethoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

530084-87-8 CA 2(1H)-Quinolinone, 8-hydroxy-5-{(1R)-1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT: THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

L4 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued) RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

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10/642,926
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=> file marpat

=> s 11 full

L5 4 SEA SSS FUL L1

=> s 15/com

L6 3 L5/COM

 $\Rightarrow$  d ibib abs fqhit 1-3

L6 ANSWER 1 OF 3
ACCESSION NUMBER:
110:15568 MARFAT
Preparation of aryl aniline .beta.-2 adrenergic
receptor agonists
Moran, Edmund J.: Jacobsen, John R.: Leadbetter,
Michael R.: Nodwell, Matthew B.: Trapp, Sean G.:
Aggen, James; Church, Timothy J.
USA
SOURCE:
USA
USA
U.S. Pat. Appl. Publ., 68 pp., Cont.-in-part of U.S.
Ser. No. 292,835.
CODEN: USXXCO
Patent TYPE:

Patent English 3 DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO. DAT	E
US 2003229058	A1	20031211	US 2003-431762 200	30508
US 6670376	B1	20031230	US 2002-292835 200	21112
US 2004059116	A1	20040325	US 2003-642926 200	30818
US 2004063755	A1	20040401	US 2003-643196 200	30818
PRIORITY APPLN. INFO.:	:		US 2001-338194P 200	11113
			US 2001-343771P 200	11228
			US 2002-292835 200:	21112
			US 2002-292211 200	21112

GI

ANSWER 1 OF 3 MARPAT COPYRIGHT 2004 ACS on STN (Continued)

= phenylene (SO (1-) G13) ,55 (1 = Ph (SO (1-) G46) = 243

243 -C (O)-G24

G44+G45= 197-6 194-1

or pharmaceutically acceptable salts and solvates additional substitution also claimed or stereoisomers

ANSWER 1 OF 3 MARPAT COPYRIGHT 2004 ACS on STN

AB Title compds. I [R1-5 = H, alk(en/yn)yl, cycloalkyl, heterocyclyl, etc.; R6 = H, alkyl, alkoxy; R7 = H, alkyl; R8 = H, alkyl; R9 = alk(en/yn)yl, (hetero)aryl, etc.; R10 = H, alkyl; R11-13 = H, (cyclo)alkyl, alkenyl, alkynyl, (hetero)aryl, etc.; p = 0-4) are prepd. For instance, the di-me ketal of 4-hydroxy-3-hydroxymethyl-alpha-bromoacetophenone (prepn. given) is reacted with 4-bromophenethylamine (CH2C12, EC3N) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NaBH4). The resulting protected amino alc. is then coupled with N-[4-heptyl-6-methyl-2-pyrimidinyl) sulfanilamice (PhMe, dppf, Pd2dba3, 80.degree., 5 h) and then deprotected with HOAC (80.degree., 5 h) to give II. All of the compds. tested demonstrated greater binding at the betal 2

adrenergic receptor than at the .beta.1 adrenergic receptor, i.e., Ki(.beta.1) > Ki(.beta.2); many with a selectivity greater than 20. I

useful for the treatment of pulmonary diseases.

= 24-9 34-16

L6 ANSWER 2 OF 3 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:401502 MARPAT
TITLE: Preparation of aryl aniline .beta.-2 adrenergic receptor agonists
INVENTOR(S): Moran, Edmund J.; Jacobsen, John R.; Leadbetter, Michael R.; Nodwell, Matthew B.; Trapp, Sean G.; Aggen, James; Church, Timothy J.
PATENT ASSIGNEE(S): Theravance, Inc, USA
POT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INPROMATION: 3

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. APPLICATION NO. DATE KIND DATE US 2003-642926 20030818 US 2001-338194P 20011113 US 2001-343771P 20011228 US 2002-292211 20021112

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L6 ANSWER 2 OF 3 MARPAT COPYRIGHT 2004 ACS on STN (Continued)

Title compds. I [R1-5 = H, alk(en/yn)yl, cycloalkyl, heterocyclyl, etc.; R6 = H, alkyl, alkoxy; R7 = H, alkyl; R8 = H, alkyl; R9 = alk(en/yn)yl, (heterolaryl, etc.; R10 = H, alkyl; R1-13 = H, (cyclo)alkyl, alkenyl, alkenyl, etc.; p = 0-4] are prepd. For instance, the di-Me ketal of 4-hydroxy-3-hydroxymethyl--alpha.-bromoacetophenone (prepn. given) is reacted with 4-bromophenethylamine (CHZC12, Et3N) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NaBH4). The resulting protected amino alc. is then coupled with N-(4-heptyl-6-methyl-2-pyrimidinyl)sulfanilamide (PhMe, dppf, Pd2dba3, 80.degree., 5 h) and then deprotected with HOAC (80.degree., 5 h) to give II. All of the compds. tested demonstrated greater binding at the a.2

adrenergic receptor than at the .beta.l adrenergic receptor, i.e., Ki(.beta.l) > Ki(.beta.2); many with a selectivity greater than 20. I

useful for the treatment of pulmonary diseases.

ANSWER 2 OF 3 MARPAT COPYRIGHT 2004 ACS on STN

MPL:

claim 1
or pharmaceutically acceptable salts and solvates
additional substitution also claimed
or stereoisomers

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE REFERENCE COUNT:

FORMAT

ANSWER 2 OF 3 MARPAT COPYRIGHT 2004 ACS on STN (Continued)

= 24-9 34-16

= phenylene (SO (1-) G13) = O = Ph (SO (1-) G46) = 243

2932-C(O)-G24

G44+G45= 197-6 194-1

```
L6 ANSWER 3 OF 3 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:401501 MARPAT
TITLE: Preparation of aryl aniline .beta.-2 adrenergic receptor agonists.
INVENTOR(S): HARBY ASSIGNEE(S): 50URCE: Theravamene, Inc., USA POT Int. Appl., 75 pp.
COODEN: PIXXD2
DOCUMENT TYPE: LANGUAGE: PAMILY ACC. NUM. COUNT: 5 Patent LANGUAGE: FAMILY ACC. NUM. COUNT: 6 PIX DE PIX 
     DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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PATENT NO.
                KIND DATE
                                APPLICATION NO. DATE
US 2003-642926
US 2001-338194P
US 2002-292211
                                            20011113
20021112
GI
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L6 ANSWER 3 OF 3 MARPAT COPYRIGHT 2004 ACS on STN (Continued)

$$\underset{R^3}{\overset{\text{OH}}{\underset{\text{H}}{\longrightarrow}}} \underset{R^4}{\overset{\text{OH}}{\underset{\text{H}}{\longrightarrow}}} \underset{R^2}{\overset{\text{N}}{\longrightarrow}} \underset{R^2}{\overset{\text{N}}{\longrightarrow}}$$

Title compds. I [R1 = methoxy, ethoxy; R2 = H, Ph or R1 = H and R2 = phenyl; R3 = CH2OH, NHCHO; R4 = H or R3-4 = taken together are NHC(0)CH=CH] are prepd. For instance, the di-Me ketal of 4-hydroxy-3-hydroxymethyl-alpha.-bromoacetophenone (prepn. given) is reacted with 4-bromophenethylamine (CH2Cl2, EtN) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NaBH4). The resulting protected amino alc. is then coupled with 4-methoxy-3-phenylaniline (PhMe, dppf, Pd2dba3, NaOBu-t, 80.degree., 5 h) and then deprotected with HOAC (80.degree., 5 h) to give II. All of the compds. tested demonstrated greater binding at the .beta.2 adrenergic receptor than at the .beta.1 adrenergic receptor, i.e., Ki(.beta.1) > Ki(.beta.2); many with a selectivity greater than 20. I are useful for the treatment of pulmonary diseases.

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L6 ANSWER 3 OF 3 MARPAT COPYRIGHT 2004 ACS On STN G1 = OMe G2 = Ph G3 +G4 = 31-8 34-7
                                                                                       (Continued)
           -сн==сн
34
뾄
             claim 1
or pharmaceutically acceptable salts or solvates
or stereoisomers
REFERENCE COUNT:
                                              THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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10/642,926
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=> d his

(FILE 'HOME' ENTERED AT 15:43:39 ON 02 JUN 2004)

FILE 'REGISTRY' ENTERED AT 15:43:43 ON 02 JUN 2004 STRUCTURE UPLOADED

L1L2 2 S L1 SAM

L3 28 S L1 FULL

FILE 'CA' ENTERED AT 15:44:10 ON 02 JUN 2004

L43 S L3

FILE 'MARPAT' ENTERED AT 15:44:44 ON 02 JUN 2004 4 S L1 FULL 3 S L5/COM

L5

L6

=>

---Logging off of STN---

Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 15:45:42 ON 02 JUN 2004